CLAIMS

WHAT IS CLAIMED IS:

1. A system comprising one or more computer processors and a computer-readable memory, the computer-readable memory comprising machine-executable code that, upon execution by the one or more computer processors, implements a method for determining a methylation profile of a cell-free deoxyribonucleic acid (cfDNA) sample from a subject, the method comprising:

a) providing conditions for converting unmethylated cytosines to uracils in nucleic acid molecules of the cfDNA sample to produce a plurality of converted nucleic acid molecules;

b) contacting the plurality of converted nucleic acids with nucleic acid probes complementary to a pre-identified methylation signature panel characteristic of at least two cell proliferative disorders, wherein the methylation signature panel comprises one or more genomic regions selected from the group consisting of genomic regions in **Tables 1-17** to enrich for sequences corresponding to the pre-identified methylation signature panel;

c) determining nucleic acid sequences of the plurality of converted nucleic acid molecules; and

d) aligning the nucleic acid sequences of the plurality of converted nucleic acid molecules to a reference nucleic acid sequence, thereby determining the methylation profile of the subject.

2. The system of claim 1, wherein the method further comprises amplifying the plurality of converted nucleic acids.

3. The system of claim 2, wherein the amplifying comprises polymerase chain reaction (PCR).

4. The system of claim 1, wherein the method further comprises preparing a nucleic acid sequencing library.

5. The system of claim 4, wherein the method further comprises amplifying the plurality of converted nucleic acids, wherein the nucleic acid sequencing library is prepared prior to amplification.

6. The system of claim 1, wherein the method further comprises determining the nucleic acid sequences of the converted nucleic acid molecules at a depth of greater than 1000x, greater than 2000x, greater than 3000x, greater than 4000x, or greater than 5000x.

7. The system of claim 1, wherein the reference nucleic acid sequence is at least a portion of a human reference genome.

8. The system of claim 1, wherein the methylation signature panel comprises three or more methylated genomic regions from the group consisting of methylated genomic regions in **Tables 1-17**, four or more methylated genomic regions from the group consisting of methylated genomic regions in **Tables 1-17**, five or more methylated genomic regions from the group consisting of methylated genomic regions in **Tables 1-17**, six or more methylated genomic regions from the group consisting of methylated genomic regions in **Tables 1-17**, seven or more methylated genomic regions from the group consisting of methylated genomic regions in **Tables 1-17**, eight or more methylated genomic regions from the group consisting of methylated genomic regions in **Tables 1-17**, nine or more methylated genomic regions from the group consisting of methylated genomic regions in **Tables 1-17**, ten or more methylated genomic regions from the group consisting of methylated genomic regions in **Tables 1-17**, eleven or more methylated genomic regions from the group consisting of methylated genomic regions in **Tables 1-17**, twelve or more methylated genomic regions from the group consisting of methylated genomic regions in **Tables 1-17**, or thirteen or more methylated genomic regions from the group consisting of methylated genomic regions in **Tables 1-17**.

9. The system of claim 1, wherein the methylation profile is associated with a cell proliferative disorder and indicative of whether a subject has a cell proliferative disorder.

10. The system of claim 1, wherein the method further comprises ligating a nucleic acid adapter comprising a unique molecular identifier to unconverted nucleic acids in the cfDNA sample prior to step a).

11. The system of claim 1, wherein the conditions for converting unmethylated cytosines to uracils in nucleic acid molecules of the cfDNA sample comprise chemical methods, enzymatic methods, or a combination thereof.

12. The system of claim 1, wherein the method further comprises treating the cfDNA sample with a reagent selected from the group consisting of bisulfite, hydrogen sulfite, disulfite, and combinations thereof.

13. The system of claim 1, wherein the cfDNA sample obtained from the subject is selected from the group consisting of body fluids, stool, colonic effluent, urine, blood plasma, blood serum, whole blood, isolated blood cells, cells isolated from the blood, and combinations thereof.

14. The system of claim 1, wherein the method further comprises applying a trained machine learning classifier to the methylation profile of the subject, wherein the trained machine learning classifier is trained to be capable of distinguishing between healthy subjects and subjects with a cell proliferative disorder to provide an output value associated with presence of a cell proliferative disorder, thereby detecting the presence or the absence of the cell proliferative disorder in the subject.

15. The system of claim 14, wherein the output value is at least 15%.

16. The system of claim 1, wherein the cell proliferative disorder is selected from the group consisting of stage 1 cancer, stage 2 cancer, stage 3 cancer, and stage 4 cancer.

17. A system comprising one or more computer processors and a computer-readable memory, the computer-readable memory comprising machine-executable code that, upon execution by the one or more computer processors, implements a method for detecting a cell proliferative disorder in a subject, the method comprising:

a) obtaining methylation sequencing information for a preselected panel of genomic regions associated with the presence of at least two different cell proliferative disorder tissue types from a nucleic acid sample from the subject,

b) applying the sequence information from the subject to a classification model trained on a preselected panel of genomic regions associated with the presence of

the at least two cell proliferative disorder types, to identify the presence of a cell proliferative disorder, and if a cell proliferative disorder is detected, and

c) applying sequence information from the subject to a classification model trained on a preselected panel of genomic regions associated with associated with the presence of cell proliferative disorders in different tissue types to determine tissue of origin of the cell proliferative disorder in the subject.

18. A system comprising one or more computer processors and a computer-readable memory, the computer-readable memory comprising machine-executable code that, upon execution by the one or more computer processors, implements a method for detecting a cell proliferative disorder in a subject, the method comprising:

a) obtaining methylation sequencing information disorders from a nucleic acid sample from the subject for a preselected panel of genomic regions associated with at least two different cell proliferative disorders,

b) calculating a methylation profile of cfDNA in the sample corresponding to the preselected panel of predetermined methylated genomic regions associated with the at least two types of cell proliferative disorders, and

c) applying a machine learning classifier trained on a panel of predetermined methylated genomic regions associated with two or more types of cell proliferative disorder, and having pre-selected sensitivity and specificity for the different types of cell proliferative disorder to be detected using the panel.

19. The system of claim 17 or 18, wherein the different types of cell proliferative disorders are selected from the group consisting of colorectal cancer, breast cancer, ovarian cancer, prostate cancer, lung cancer, pancreatic cancer, uterine cancer, liver cancer, esophagus cancer, stomach cancer, thyroid cancer, or bladder cancer.

20. The system of claim 17 or 18, wherein the machine learning classifier is tailored to provide pre-selected sensitivity and specificity for the different types of cell proliferative disorder to be detected depending on needs of cancer diagnosis and confirmatory diagnosis for two or more cancers selected from the group consisting of colorectal cancer, breast cancer, ovarian cancer, prostate cancer, lung cancer, pancreatic cancer, uterine

cancer, liver cancer, esophagus cancer, stomach cancer, thyroid cancer, and bladder cancer,

wherein the pre-selected sensitivity for a colorectal cancer associated classification panel is at least 70% sensitivity; the pre-selected specificity for a breast cancer associated classification panel is at least 70% specificity; the pre-selected specificity for an ovarian cancer associated classification panel is at least 90% specificity; the pre-selected specificity for a prostate cancer associated classification panel is at least 70% specificity; the pre-selected specificity for a lung cancer associated classification panel is at least 70% specificity; the pre-selected specificity for a pancreatic cancer associated classification panel is at least 90% specificity; the pre-selected specificity for a uterine cancer associated classification panel is at least 90% specificity; the pre-selected sensitivity for a liver cancer associated classification panel is at least 70% sensitivity; the pre-selected sensitivity for an esophagus cancer associated classification panel is at least 70% sensitivity; the pre-selected sensitivity for a stomach cancer associated classification panel is at least 70% sensitivity; the pre-selected specificity for a thyroid cancer associated classification panel is at least 70% specificity; and the pre-selected sensitivity for a bladder cancer associated classification panel is at least 70% sensitivity selected based on which cancer types are detected by the classification model.

21. A system comprising one or more computer processors and a computer-readable memory, the computer-readable memory comprising machine-executable code that, upon execution by the one or more computer processors, implements a method for detecting a presence or an absence of a cell proliferative disorder in a subject, the method comprising:

a) providing conditions for converting unmethylated cytosines to uracils in nucleic acid molecules of a biological sample obtained or derived from the subject to produce a plurality of converted nucleic acid molecules;

b) contacting the plurality of converted nucleic acids with nucleic acid probes complementary to a pre-identified methylation signature panel of at least two differentially methylated regions selected from the group consisting of **Tables 1-17** to enrich for sequences corresponding to the signature panel;

c) determining nucleic acid sequences of the converted nucleic acid molecules;

d) aligning the nucleic acid sequences of the plurality of converted nucleic acid molecules to a reference nucleic acid sequence, thereby determining a methylation profile of the subject; and

e) applying a trained machine learning classifier to the methylation profile, wherein the trained machine learning classifier is trained to be capable of distinguishing between healthy subjects and subjects with a cell proliferative disorder to provide an output value associated with presence of a cell proliferative disorder, thereby detecting the presence or the absence of the cell proliferative disorder in the subject.

22. A system comprising one or more computer processors and a computer-readable memory, the computer-readable memory comprising machine-executable code that, upon execution by the one or more computer processors, implements a method for detecting a cell proliferative disorder in a subject, the method comprising:

a) providing conditions for converting unmethylated cytosines to uracils in nucleic acid molecules of a cfDNA sample to produce a plurality of converted nucleic acids;

b) amplifying converted nucleic acids with polymerase chain reaction;

c) probing the converted nucleic acids with nucleic acid probes complementary to a pre-identified methylation signature panel of at least two differentially methylated regions selected from the group consisting of **Tables 1-17** to enrich for sequences corresponding to the signature panel;

d) determining the nucleic acid sequence of the converted nucleic acid molecules at a depth of greater than 5000x, and

e) aligning the nucleic acid sequence of the converted nucleic acid molecules to a reference nucleic acid sequence for the pre-identified panel of CpG loci, to determine the methylation profile of the subject, and

f) analyzing the methylation profile using a machine learning model trained to be capable of distinguishing between healthy subjects and subjects with a cell proliferative disorder to provide an output value associated with presence of a cell

proliferative disorder, thereby indicating the presence of a cell proliferative disorder in the subject.

23. The system of claim 21 or 22, wherein the biological sample obtained from the subject is selected from the group consisting of body fluids, stool, colonic effluent, urine, blood plasma, blood serum, whole blood, isolated blood cells, cells isolated from the blood, and combinations thereof.

24. The system of claim 21 or 22, wherein the method comprises applying the measured methylation signature panel from the subject against a database of measured methylation signature panels from normal subjects, wherein the database is stored on a computer system; determining that the subject has an increased risk of having a cell proliferative disorder by measuring a change of at least 15% in the methylation status of the methyl signature panel relative to methylation status from normal subjects.

25. The system of claim 21 or 22, wherein the cell proliferative disorder is selected from the group consisting of stage 1 cancer, stage 2 cancer, stage 3 cancer, and stage 4 cancer.

26. The system of claim 21 or 22, wherein the method detects pancreatic cancer and is performed in combination with detecting the presence or amount of CA19-9 protein in the biological sample.

27. The system of claim 21 or 22, wherein the method detects prostate cancer and is performed in combination with detecting the presence or amount of PSA protein in the biological sample.

28. A methylation signature panel characteristic of at least two cell proliferative disorders comprising:

one or more genomic regions selected from the group consisting of genomic regions in **Table 1**, wherein the one or more genomic regions are more methylated in a biological sample from a subject having a cell proliferative disorder or subtype thereof, and are less methylated in a biological sample from a subject not having the cell proliferative disorder or subtype thereof.

29. The methylation signature panel of claim 28, wherein the biological sample is a nucleic acid, DNA, RNA, or cell-free nucleic acid.

30. The methylation signature panel of claim 28, wherein the one or more genomic regions are non-coding regions, coding regions, non-transcribed regions, or regulator regions.

31. The methylation signature panel of claim 28, wherein the methylation signature panel comprises six or more genomic regions selected from the group consisting of genomic regions in **Table 1**.

32. The methylation signature panel of claim 28, wherein the one or more genomic regions selected from the group consisting of genomic regions in **Table 1** is associated with a type of cancer.

33. The methylation signature panel of claim 28, wherein the biological sample obtained from the subject having the cell proliferative disorder or subtype thereof is selected from the group consisting of body fluids, stool, colonic effluent, urine, blood plasma, blood serum, whole blood, isolated blood cells, cells isolated from the blood, and combinations thereof.

34. The methylation signature panel of claim 28, wherein the biological sample obtained from the subject not having the cell proliferative disorder or subtype thereof is selected from the group consisting of body fluids, stool, colonic effluent, urine, blood plasma, blood serum, whole blood, isolated blood cells, cells isolated from the blood, and combinations thereof.

35. The methylation signature panel of claim 28, wherein the cell proliferative disorder is selected from the group consisting of colorectal cell proliferation, prostate cell proliferation, lung, breast cell proliferation, pancreatic cell proliferation, ovarian cell proliferation, uterine cell proliferation, liver cell proliferation, esophagus cell proliferation, stomach cell proliferation, and thyroid cell proliferation.

36. The methylation signature panel of claim 28, wherein the cell proliferative disorder is selected from the group consisting of colon adenocarcinoma, liver hepatocellular carcinoma, lung adenocarcinoma, lung squamous cell carcinoma, ovarian serious cystadenocarcinoma, pancreatic adenocarcinoma, prostate adenocarcinoma, and rectum adenocarcinoma.

37. The methylation signature panel of claim 28, wherein the cell proliferative disorder is selected from the group consisting of stage 1 cancer, stage 2 cancer, stage 3 cancer, and stage 4 cancer.

38. The methylation signature panel of claim 28, wherein the signature panel comprises two or more genomic regions selected from the group consisting of genomic regions in **Table 1**, three or more genomic regions selected from the group consisting of genomic regions in **Table 1**, four or more genomic regions selected from the group consisting of genomic regions in **Table 1**, five or more genomic regions selected from the group consisting of genomic regions in **Table 1**, six or more genomic regions selected from the group consisting of genomic regions in **Table 1**, seven or more genomic regions selected from the group consisting of genomic regions in **Table 1**, eight or more methylated genomic regions selected from the group consisting of genomic regions in **Table 1**, nine or more genomic regions selected from the group consisting of genomic regions in **Table 1**, ten or more genomic regions selected from the group consisting of genomic regions in **Table 1**, eleven or more genomic regions in genomic regions in **Table 1**, twelve or more genomic regions selected from the group consisting of genomic regions in **Table 1**, or thirteen or more genomic regions selected from the group consisting of genomic regions in **Table 1**.

39. A methylation signature panel characteristic of a tissue of origin for at least two cell proliferative disorders comprising:

two or more genomic regions selected from the group consisting of genomic regions in **Tables 2-17**, wherein the two or more genomic regions are more methylated in a biological sample from a subject having a cell proliferative disorder or subtype thereof, and are less methylated in a biological sample from a subject not having the cell proliferative disorder or subtype thereof.

40. The methylation signature panel of claim 39, wherein the biological sample is a nucleic acid, DNA, RNA, or cell-free nucleic acid.

41. The methylation signature panel of claim 39, wherein the two or more genomic regions are non-coding regions, coding regions, non-transcribed regions, or regulator regions.

42. The methylation signature panel of claim 39, wherein the methylation signature panel comprises six or more genomic regions selected from the group consisting of genomic regions in **Tables 2-17**.

43. The methylation signature panel of claim 39, wherein the one or more genomic regions selected from the group consisting of genomic regions in **Tables 2-17** are associated with a type of cancer and a tumor tissue-of-origin.

44. The methylation signature panel of claim 39, wherein the biological sample obtained from the subject having the cell proliferative disorder or subtype thereof is selected from the group consisting of body fluids, stool, colonic effluent, urine, blood plasma, blood serum, whole blood, isolated blood cells, cells isolated from the blood, and combinations thereof.

45. The methylation signature panel of claim 39, wherein the biological sample obtained from the subject not having the cell proliferative disorder or subtype thereof is selected from the group consisting of body fluids, stool, colonic effluent, urine, blood plasma, blood serum, whole blood, isolated blood cells, cells isolated from the blood, and combinations thereof.

46. The methylation signature panel of claim 39, wherein cell proliferative disorder is selected from the group consisting of colorectal cell proliferation, prostate cell proliferation, lung cell proliferation, breast cell proliferation, pancreatic cell proliferation, ovarian cell proliferation, uterine cell proliferation, liver cell proliferation, esophagus cell proliferation, stomach cell proliferation, or thyroid cell proliferation.

47. The methylation signature panel of claim 39, wherein the cell proliferative disorder is selected from the group consisting of colon adenocarcinoma, liver hepatocellular carcinoma, lung adenocarcinoma, lung squamous cell carcinoma, ovarian serious cystadenocarcinoma, pancreatic adenocarcinoma, prostate adenocarcinoma, and rectum adenocarcinoma.

48. The methylation signature panel of claim 39, wherein cell proliferative disorder is selected from the group consisting of stage 1 cancer, stage 2 cancer, stage 3 cancer, and stage 4 cancer.

49. The methylation signature panel of claim 39, wherein signature panel comprises three or more genomic regions selected from the group consisting of genomic regions in **Tables 2-17**, four or more genomic regions selected from the group consisting of genomic regions in **Tables 2-17**, five or more genomic regions selected from the group consisting of genomic regions in **Tables 2-17,** six or more genomic regions selected from the group consisting of genomic regions in **Tables 2-17**, seven or more genomic regions selected from the group consisting of genomic regions in **Tables 2-17**, eight or more genomic regions selected from the group consisting of genomic regions in **Tables 2-17**, nine or more genomic regions selected from the group consisting of genomic regions in **Tables 2-17**, ten or more genomic regions selected from the group consisting of genomic regions in **Tables 2-17**, eleven or more genomic regions in genomic regions in **Tables 2-17**, twelve or more genomic regions selected from the group consisting of genomic regions in **Tables 2-17**, or thirteen or more genomic regions selected from the group consisting of genomic regions in **Tables 2-17**.

50. The methylation signature panel of claim 39, wherein the at least two cell proliferative disorders comprise a combination selected from the group consisting of: colorectal cancer and prostate cancer; colorectal cancer and lung cancer; colorectal cancer and breast cancer; colorectal cancer and liver cancer; colorectal cancer and ovarian cancer; colorectal cancer and pancreatic cancer; prostate cancer and lung cancer; prostate cancer and breast cancer; prostate cancer and liver cancer; prostate cancer and ovarian cancer; prostate cancer and pancreatic cancer; lung cancer and breast cancer; lung cancer and liver cancer; lung cancer and ovarian cancer; lung cancer and pancreatic cancer; breast cancer and liver cancer; breast cancer and ovarian cancer; breast cancer and pancreatic cancer; liver cancer and ovarian cancer; liver cancer and pancreatic cancer; ovarian cancer and pancreatic cancer; colorectal cancer, prostate cancer, and lung cancer; colorectal cancer, prostate cancer, and breast cancer; colorectal cancer, prostate cancer, and liver cancer; colorectal cancer, prostate cancer, and ovarian cancer; colorectal cancer, prostate cancer, and pancreatic cancer; colorectal cancer, lung cancer, and breast cancer; colorectal cancer, lung cancer, and liver cancer; colorectal cancer, lung cancer, and ovarian cancer; colorectal cancer, lung cancer, and pancreatic cancer; colorectal cancer, breast cancer, and liver cancer; colorectal cancer, breast cancer, and ovarian cancer;

colorectal cancer, breast cancer, and pancreatic cancer; prostate cancer, liver cancer, and ovarian cancer; prostate cancer, liver cancer, and pancreatic cancer; prostate cancer, ovarian cancer, and pancreatic cancer; and colorectal cancer, prostate cancer, lung cancer, and breast cancer.

51. The methylation signature panel of claim 39, wherein the two or more genomic regions are selected from the group consisting of genomic regions in **Tables 2**, **3**, and **4**, and are associated with a colorectal cancer tissue of origin.

52. The methylation signature panel of claim 39, wherein the two or more genomic regions are selected from the group consisting of genomic regions in **Tables 5**, **6**, and **7**, and are associated with a liver cancer tissue of origin.

53. The methylation signature panel of claim 39, wherein the two or more genomic regions are selected from the group consisting of genomic regions in **Tables 8** and **9**, and are associated with a lung cancer tissue of origin.

54. The methylation signature panel of claim 39, wherein the two or more genomic regions are selected from the group consisting of genomic regions in **Tables 10**, **11**, and **12**, and are associated with an ovarian cancer tissue of origin.

55. The methylation signature panel of claim 39, wherein the panel of two or more genomic regions are selected from the group consisting of genomic regions in **Tables 13** and **14**, and are associated with a pancreatic cancer tissue of origin.

56. The methylation signature panel of claim 39, wherein the two or more genomic regions are selected from the group consisting of genomic regions in **Tables 15**, **16**, and **17**, and are associated with a prostate cancer tissue of origin.

57. A machine learning classifier capable of distinguishing a population of healthy subjects from subjects having a cell proliferative disorder, comprising:

a) sets of measured values representative of differentially-methylated genomic regions of the group consisting of differentially-methylated genomic regions in **Tables 1-17**, wherein the differentially-methylated genomic regions are associated with at least two cell proliferative disorders, where the measured values are obtained from

methylation sequencing data from healthy subjects and subjects having a cell proliferative disorder,

b) wherein the measured values are used to generate a set of features corresponding to properties of the differentially-methylated genomic regions and where the features are analyzed using a machine learning or statistical model,

c) wherein the model provides a feature vector useful as a classifier capable of distinguishing a population of healthy subjects from subjects having a cell proliferative disorder.

58. The machine learning classifier of claim 57, wherein the sets of measured values describe characteristics of the methylated regions selected from the group consisting of: base wise methylation percent for CpG, CHG, CHH; the count or rate of observing fragments with different counts or rates of methylated CpGs in a region; conversion efficiency (100-mean methylation percent for CHH); hypomethylated blocks; methylation levels (global mean methylation for CPG, CHH, CHG, fragment length, fragment midpoint, and methylation levels in one or more genomic regions such as chrM, LINE1, or ALU); number of methylated CpGs per fragment; fraction of CpG methylation to total CpG per fragment; fraction of CpG methylation to total CpG per region; fraction of CpG methylation to total CpG in panel; dinucleotide coverage (normalized coverage of dinucleotide); evenness of coverage (unique CpG sites at lx and 10x mean genomic coverage (for S4 runs); mean CpG coverage (depth) globally; and mean coverage at CpG islands, CGI shelves, and CGI shores.

59. The machine learning classifier of claim 57, wherein machine learning classifier is capable of identifying a tissue of origin of a tumor in the subject.

60. The machine learning classifier of claim 57, wherein the classifier is loaded into a memory of a computer system, wherein the model is trained using training vectors obtained from training biological samples, a first subset of the training biological samples identified as having a cell proliferative disorder, and a second subset of the training biological samples identified as not having a cell proliferative disorder.

61. A machine learning classifier of claim 57, wherein the model is trained on a panel of predetermined methylated genomic regions associated with at least two cell proliferative

disorders, and having pre-selected sensitivity and specificity for the different types of cell proliferative disorder to be detected using the panel.

62. The machine learning classifier of claim 57, wherein the at least two cell proliferative disorders are selected from the group consisting of colorectal cancer, breast cancer, ovarian cancer, prostate cancer, lung cancer, pancreatic cancer, uterine cancer, liver cancer, esophagus cancer, stomach cancer, thyroid cancer, and bladder cancer.

63. The machine learning classifier of claim 57, wherein the machine learning classifier is tailored to provide a pre-selected sensitivity and a pre-selected specificity for each of the at least two cell proliferative disorders, wherein the at least two cell proliferative disorders are selected from the group consisting of colorectal cancer, breast cancer, ovarian cancer, prostate cancer, lung cancer, pancreatic cancer, uterine cancer, liver cancer, esophagus cancer, stomach cancer, thyroid cancer, and bladder cancer,

wherein the pre-selected sensitivity for a colorectal cancer associated classification panel is at least 70% sensitivity; the pre-selected specificity for a breast cancer associated classification panel is at least 70% specificity; the pre-selected specificity for an ovarian cancer associated classification panel is at least 90% specificity; the pre-selected specificity for a prostate cancer associated classification panel is at least 70% specificity; the pre-selected specificity for a lung cancer associated classification panel is at least 70% specificity; the pre-selected specificity for a pancreatic cancer associated classification panel is at least 90% specificity; the pre-selected specificity for a uterine cancer associated classification panel is at least 90% specificity; the pre-selected sensitivity for a liver cancer associated classification panel is at least 70% sensitivity; the pre-selected sensitivity for an esophagus cancer associated classification panel is at least 70% sensitivity; the pre-selected sensitivity for a stomach cancer associated classification panel is at least 70% sensitivity; the pre-selected specificity for a thyroid cancer associated classification panel is at least 70% specificity; and the pre-selected sensitivity for a bladder cancer associated classification panel is at least 70% sensitivity selected based on which cancer types are detected by the classification model.

64. A system comprising a machine learning model classifier for detecting a cell proliferative disorder, comprising:

a) a computer-readable medium comprising a classifier operable to classify subjects as having the cell proliferative disorder or not having the cell proliferative disorder based on a methylation signature panel of one or more genomic regions selected from the group consisting of genomic regions in **Tables 1-17**; and

b) one or more processors for executing instructions stored on the computer-readable medium.

65. The system of claim 64, wherein the system comprises the classifier loaded into a memory of a computer system, the machine learning model trained using training vectors obtained from training biological samples, a first subset of the training biological samples identified as having a cell proliferative disorder and a second subset of the training biological samples identified as not having a cell proliferative disorder.

66. The system of claim 64, wherein the classifier is provided in a system for detecting a cell proliferative disorder comprising:

a) a computer-readable medium comprising a classifier operable to classify the subjects based on a methylation signature panel described herein; and

b) one or more processors for executing instructions stored on the computer-readable medium.

67. The system of claim 64, wherein the system comprises a classification circuit that is configured as a machine learning classifier selected from the group consisting of a deep learning classifier, a neural network classifier, a linear discriminant analysis (LDA) classifier, a quadratic discriminant analysis (QDA) classifier, a support vector machine (SVM) classifier, a random forest (RF) classifier, a linear kernel support vector machine classifier, a first or second order polynomial kernel support vector machine classifier, a ridge regression classifier, an elastic net algorithm classifier, a sequential minimal optimization algorithm classifier, a naive Bayes algorithm classifier, and principal component analysis classifier.

68. The system of claim 64, wherein the computer-readable medium is a non-transitory computer-readable medium comprising machine-executable code that, upon execution by one or more computer processors, implements any of the methods above or elsewhere herein.

69. The system of claim 64, wherein the system comprises one or more computer processors and computer memory coupled thereto, wherein the computer memory comprises machine-executable code that, upon execution by the one or more computer processors, implements a method for detecting a cell proliferative disorder.

70. A system comprising one or more computer processors and a computer-readable memory, the computer-readable memory comprising machine-executable code that, upon execution by the one or more computer processors, implements a method for monitoring minimal residual disease in a subject previously treated for disease, the method comprising:

determining a methylation profile as described herein as a baseline methylation state and repeating an analysis to determine the methylation profile at one or more predetermined time points wherein a change from baseline indicates a change in the minimal residual disease status at baseline in the subject.

71. The system of claim 70, wherein the minimal residual disease is selected from the group consisting of response to treatment, tumor load, residual tumor post-surgery, relapse, secondary screen, primary screen, and cancer progression.

72. The system of claim 70, wherein the method is for determining response to treatment.

73. The system of claim 70, wherein the method is for monitoring tumor load.

74. The system of claim 70, wherein the method is for detecting residual tumor post-surgery.

75. The system of claim 70, wherein the method is for detecting relapse.

76. The system of claim 70, wherein the method is for use as a secondary screen.

77. The system of claim 70, wherein the method is for use as a primary screen.

78. The system of claim 70, wherein the method is for monitoring cancer progression.

79. The system of claim 70, wherein the dataset is indicative of the presence or susceptibility of the cancer at a sensitivity of at least about 80%.

80. The system of claim 70, wherein the dataset is indicative of the presence or susceptibility of the cancer at a sensitivity of at least about 90%.

81. The system of claim 70, wherein the dataset is indicative of the presence or susceptibility of the cancer at a sensitivity of at least about 95%.

82. The system of claim 70, wherein the dataset is indicative of the presence or susceptibility of the cancer at a positive predictive value (PPV) of at least about 70%.

83. The system of claim 70, wherein the dataset is indicative of the presence or susceptibility of the cancer at a positive predictive value (PPV) of at least about 80%.

84. The system of claim 70, wherein the dataset is indicative of the presence or susceptibility of the cancer at a positive predictive value (PPV) of at least about 90%.

85. The system of claim 70, wherein the dataset is indicative of the presence or susceptibility of the cancer at a positive predictive value (PPV) of at least about 95%.

86. The system of claim 70, wherein the dataset is indicative of the presence or susceptibility of the cancer at a positive predictive value (PPV) of at least about 99%.

87. The system of claim 70, wherein the dataset is indicative of the presence or susceptibility of the cancer at a negative predictive value (NPV) of at least about 80%.

88. The system of claim 70, wherein the dataset is indicative of the presence or susceptibility of the cancer at a negative predictive value (NPV) of at least about 90%.

89. The system of claim 70, wherein the dataset is indicative of the presence or susceptibility of the cancer at a negative predictive value (NPV) of at least about 95%.

90. The system of claim 70, wherein the dataset is indicative of the presence or susceptibility of the cancer at a negative predictive value (NPV) of at least about 99%.

91. The system of claim 70, wherein the trained algorithm determines the presence or susceptibility of the cancer of the subject with an Area Under Curve (AUC) of at least about 0.90.

92. The system of claim 70, wherein the trained algorithm determines the presence or susceptibility of the cancer of the subject with an Area Under Curve (AUC) of at least about 0.95.

93. The system of claim 70, wherein the trained algorithm determines the presence or susceptibility of the cancer of the subject with an Area Under Curve (AUC) of at least about 0.99.

94. The system of claim 70, wherein the method further comprises presenting a report a graphical user interface of an electronic device of a user.

95. The system of claim 70, wherein the user is the subject, individual or patient.

96. The system of claim 70, wherein the method further comprises determining a likelihood of the determination of a presence or susceptibility of cancer in the subject, individual, or patient.

97. The system of claim 70, wherein the trained algorithm comprises a supervised machine learning algorithm.

98. The system of claim 70, wherein the supervised machine learning algorithm comprises a deep learning algorithm, a support vector machine (SVM), a neural network, or a Random Forest.